201-14522

**NCIC HPV**
Sent by: Mary-Beth Weaver

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To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on 4-Nitro-N-Methylphthalimide (CAS# 41663-84-7)

Richard_Denison@environmentaldefense.org on 05/30/2003 09:53:43 AM

To: oppt.ncic@epamail.epa.gov, hpv.chemrtk@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, Ronald.Joiner@GEP.GE.COM
cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org

Subject: Environmental Defense comments on 4-Nitro-N-Methylphthalimide (CAS# 41663-84-7)

(Submitted via Internet 5/30/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and Ronald.Joiner@GEP.GE.COM)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 4-Nitro-N-Methylphthalimide (CAS# 41663-84-7).

The test plan and robust summary for 4-Nitro-N-Methylphthalimide (4-NPI) were prepared by the General Electric Company. Overall, the robust summaries were informative and written in an objective manner. The test plan itself did not attempt to summarize the rationale for the specifics of the test plan, nor did it provide any information on actual or potential human or environmental exposures for 4-NPI. According to the sponsor, 4-NPI is used as a site-limited intermediate to make high-molecular-weight polyetherimide polymers, although no information was provided on its presence or absence in consumer products and workplace exposure and safety issues were not addressed by the test plan.

The sponsor proposes to conduct additional studies on environmental fate and transport endpoints and a reproductive toxicity study in order to fill data gaps for these endpoints. We agree with the proposals made by the sponsor for additional testing and do not recommend any testing on 4-NPI beyond that proposed. Specific comments are as follows:

1. There are no existing studies on photodegradation, transport and distribution or biodegradation. Accordingly, the sponsor proposes studies on these endpoints and we agree that such studies should be conducted.

2. The ecotoxicity studies were well-conducted and clearly described in the robust summaries; we agree that no additional ecotoxicity studies are needed to fulfill HPV endpoints.

3. The genetic toxicity studies gave mixed results; in vivo chromosomal aberration studies were negative but in vitro studies were, in some cases, positive. Metabolic activation does appear to play a role in the mutation mechanism of 4-NPI. Although the results of genetic toxicity testing are difficult to interpret, the studies were well-conducted and described, so we consider them adequate to fulfill requirements of the HPV program. It would be helpful, however, if the sponsor conducted additional mechanistic studies for the purpose of gaining a clearer understanding of the genetic toxicity of 4-NPI. Of particular interest is the identification of the 4-NPI metabolite(s) responsible for the observed genotoxic activity.

4. The repeat dose and developmental toxicity studies were of good quality

and need not be repeated. However, there are no available studies on reproductive toxicity. Since 4-NPI does cause some teratogenic responses, we agree with the sponsor's proposal to conduct a reproductive toxicity study.

Thank you for this opportunity to comment.

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